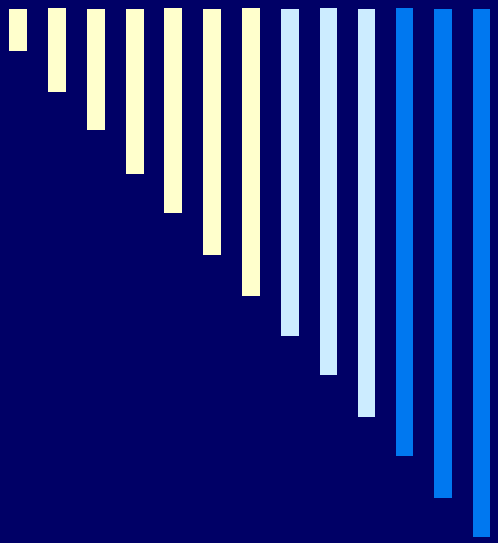

Preventing unsafe abortion

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Geneva Foundation for Medical Education and Research

March 2004

Definition of Terms

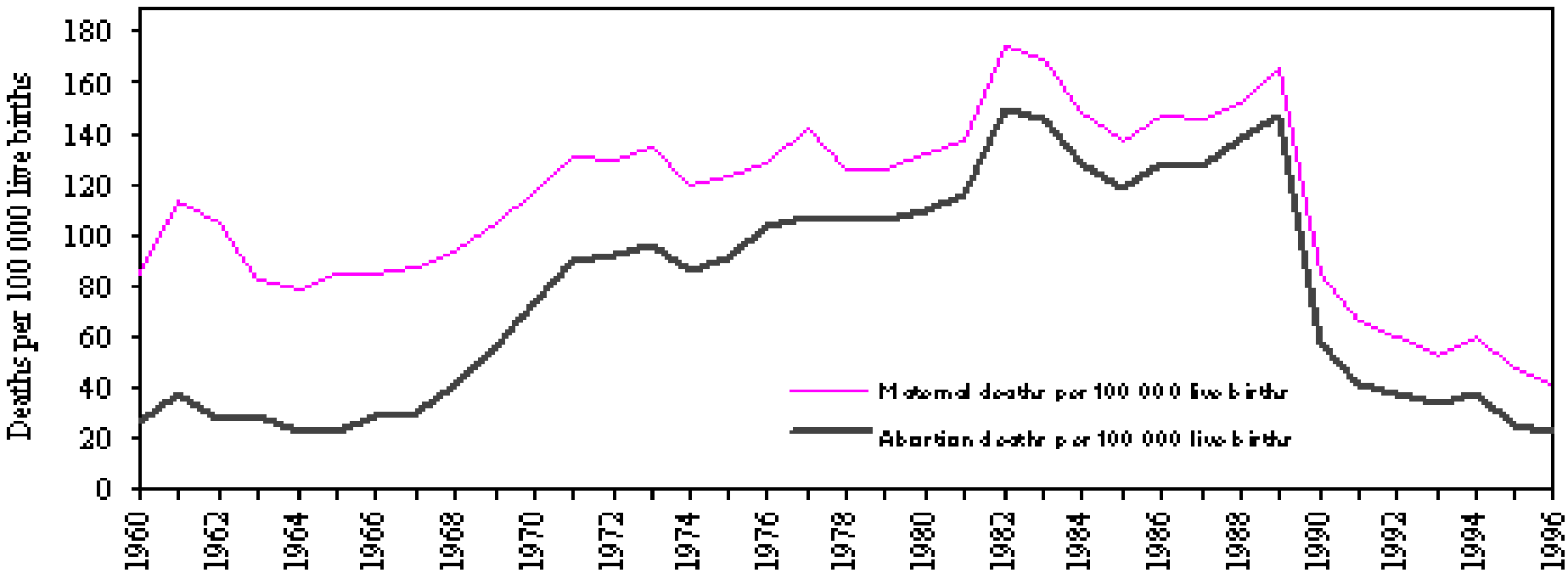
- "abortion" refers to the termination of pregnancy from whatever cause before the fetus is capable of extrauterine life.
- “spontaneous abortion" refers to those terminated pregnancies that occur without deliberate measures
- "induced abortion" refers to termination of pregnancy through a deliberate intervention intended to end the pregnancy (WHO, 1994).

Definition of unsafe abortion

- **"...a procedure for terminating unwanted pregnancy either by persons lacking the necessary skills or in an environment lacking the minimal medical standards of both"** which therefore exposes the women to an increased risk of morbidity and mortality.

(WHO,1993)

Effects of the introduction of the anti-abortion law in Romania (1966)



Unsafe abortion - consequences

- Morbidity, mortality
- Health care sector

Data collection

- Hospital admissions for complications
- Community surveys
- Abortion providers' surveys
- Mortality studies

- Unsafe abortion database

Global annual estimates of incidence and mortality for unsafe abortions 1995-2000

(WHO, 2000)

	World total	Africa	Asia	Europe	Latin America
Incidence rate (*unsafe abortions per 1 000 women 15-49)*	13	27	11	5	30
Incidence ratio (*unsafe abortions per 100 live births)*	15	16	13	12	36
Estimated number of deaths due to unsafe abortion	78 000	34 000	38 500	500	5000
Proportion of maternal deaths (*% of maternal deaths due to unsafe abortion*)	13	13	12	17	21

Methods

- Surgical
- Non-surgical
- Menstrual regulation (MR)
  - generally used to describe early evacuation of the uterus, after a delayed menses, often without confirmation of pregnancy

Medical methods

- Prostaglandin
- Mifepristone
- Combination, dose, route

- Methotrexate
- Tamoxifen

Antigestagen

- Developed during 1960s
- Mifepristone (RU 486)
  - Suppression of folliculogenesis and ovulation
  - endometrium
- Receptors
  - Progesteron
  - Glucocorticoid

Mifepristone

- Action
  - endometrium
  - uterus
  - cervix
- Pharmacokinetics
  - Linear 2-25 mg/day
  - Non-linear above 100 mg/day

Misoprostol, Gemeprost

- Prostaglandin E1 + E2
- Effectiveness: < 90%
- Side effects

Strategy - Cochrane systematic review

- Randomised controlled trials
- Critical appraisal
- Meta - analysis where appropriate
- Search and methods according to Cochrane Fertility Regulation Group Guidelines

Approach

- Pregnant women, first trimester (<14 wks)
- Interventions
  - Medical
  - Surgical
  - Medical vs Surgical
- Outcomes
  - effectiveness, complications, side effects, acceptability

Medical abortion – structure of the review

- Combined regime: mifepristone/prostaglandin
  - Dose, route, time of administration, type of PG, split dose
- Combined regime: methotrexate/prostaglandin
  - Dose, route, timing
- Single vs combined regime
- Others
  - Tamoxifen, laminaria etc

- 14 main comparisons

Medical methods

Kulier 2004

- Systematic review
- 39 trials included
- 14 main comparisons
- Main outcome: effectiveness

Medical methods Kulier 2004

Combination:

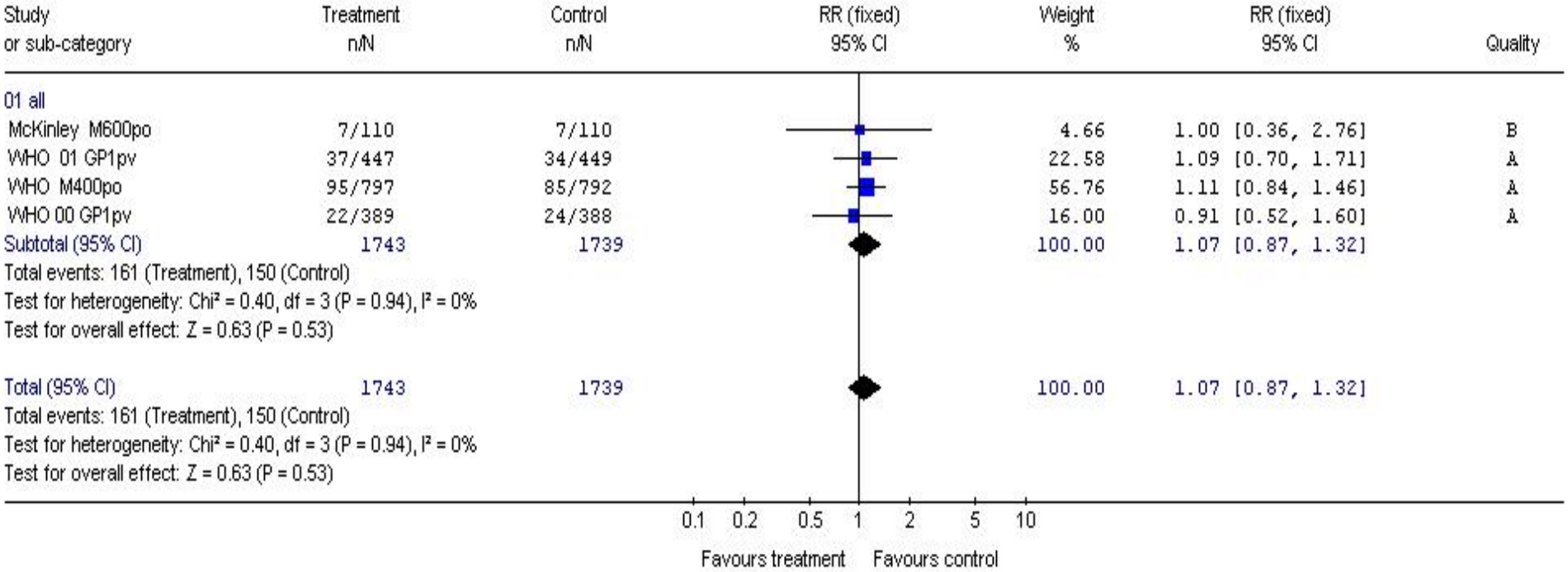
Mifepristone 200 – 600 mg
followed by
Prostaglandin
- Type
- Dose
- Route
- Time interval

Medical methods

dose of mifepristone

Kulier 2004

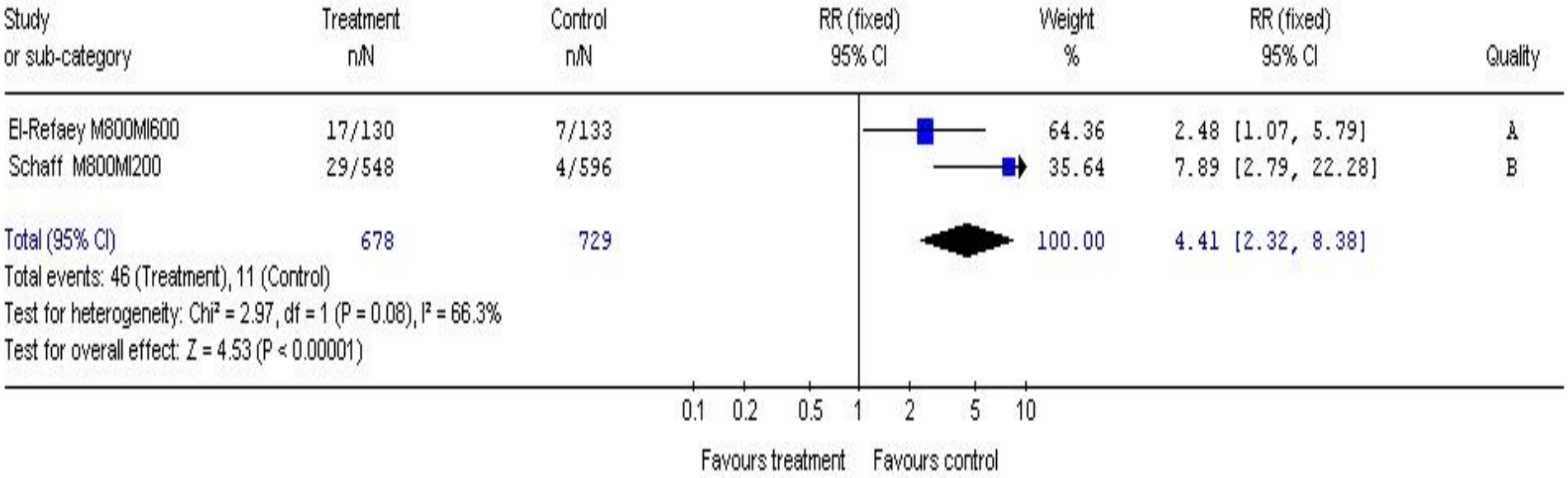
Review: Medical methods for first trimester abortion
Comparison: 01 combined regimen mifepristone/prostaglandin: dose of mifepristone: 600mg vs 200mg
Outcome: 01 failure to achieve complete abortion



Medical methods Kulier 2004

misoprostol po vs pv

Review: Medical methods for first trimester abortion
Comparison: 05 combined regimen mifepristone/prostaglandin: misoprostol po vs pv
Outcome: 01 failure to achieve complete abortion

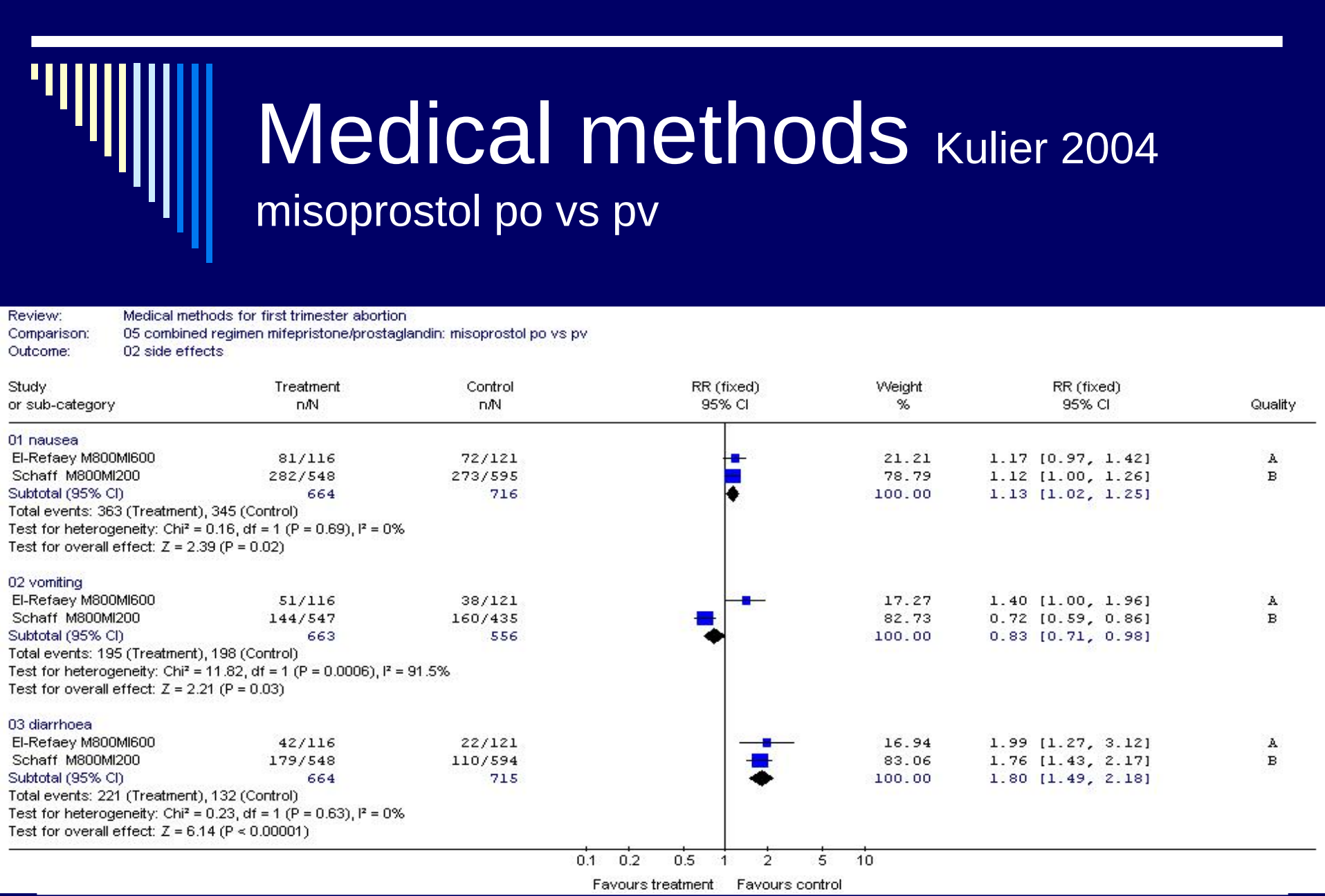


Medical methods Kulier 2004

misoprostol po vs pv

Review: Medical methods for first trimester abortion
Comparison: 05 combined regimen mifepristone/prostaglandin: misoprostol po vs pv
Outcome: 02 side effects

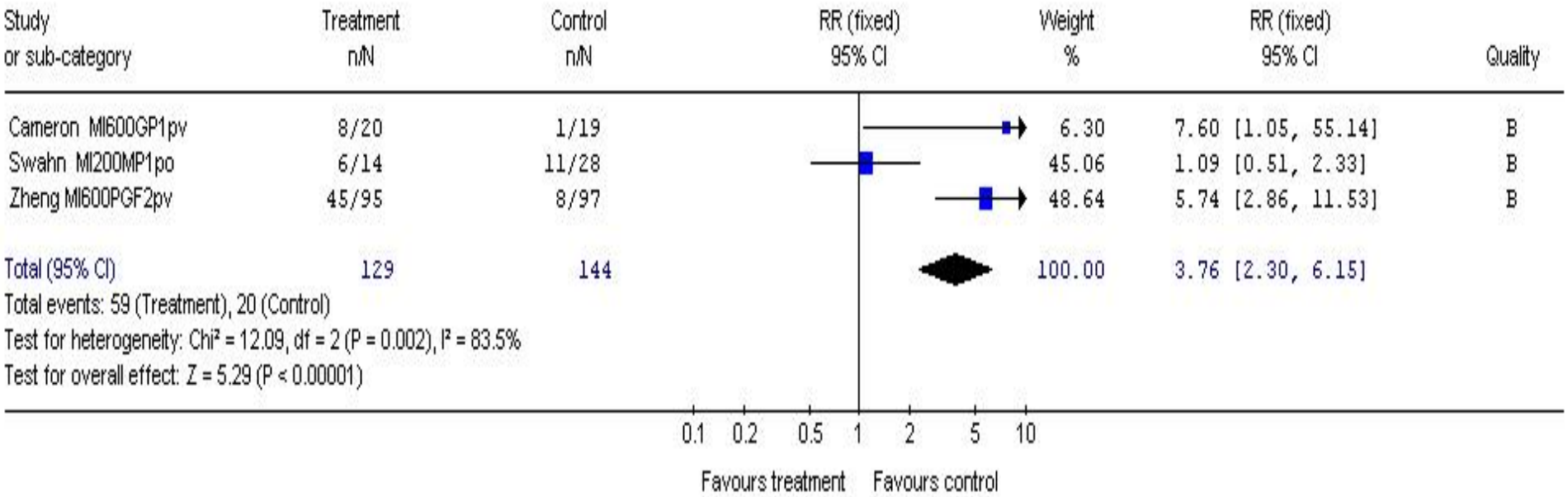
Study or sub-category	Treatment n/N	Control n/N	RR (fixed) 95% CI	Weight %	RR (fixed) 95% CI	Quality
01 nausea						
El-Refaey M800MI600	81/116	72/121		21.21	1.17 [0.97, 1.42]	A
Schaff M800MI200	282/548	273/595		78.79	1.12 [1.00, 1.26]	B
Subtotal (95% CI)	664	716		100.00	1.13 [1.02, 1.25]	
Total events: 363 (Treatment), 345 (Control)						
Test for heterogeneity: Chi² = 0.16, df = 1 (P = 0.69), I² = 0%						
Test for overall effect: Z = 2.39 (P = 0.02)						
02 vomiting						
El-Refaey M800MI600	51/116	38/121		17.27	1.40 [1.00, 1.96]	A
Schaff M800MI200	144/547	160/435		82.73	0.72 [0.59, 0.86]	B
Subtotal (95% CI)	663	556		100.00	0.83 [0.71, 0.98]	
Total events: 195 (Treatment), 198 (Control)						
Test for heterogeneity: Chi² = 11.82, df = 1 (P = 0.0006), I² = 91.5%						
Test for overall effect: Z = 2.21 (P = 0.03)						
03 diarrhoea						
El-Refaey M800MI600	42/116	22/121		16.94	1.99 [1.27, 3.12]	A
Schaff M800MI200	179/548	110/594		83.06	1.76 [1.43, 2.17]	B
Subtotal (95% CI)	664	715		100.00	1.80 [1.49, 2.18]	
Total events: 221 (Treatment), 132 (Control)						
Test for heterogeneity: Chi² = 0.23, df = 1 (P = 0.63), I² = 0%						
Test for overall effect: Z = 6.14 (P < 0.00001)						



Medical methods Kulier 2004

mifepristone alone vs combined

Review: Medical methods for first trimester abortion
Comparison: 07 mifepristone alone vs combined regimen mifepristone/prostaglandin
Outcome: 01 failure to achieve complete abortion



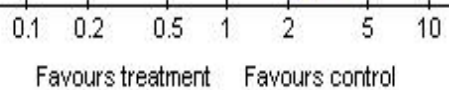
Medical methods

prostaglandin vs combined regime

Kulier 2004

Review: Medical methods for first trimester abortion
Comparison: 08 prostaglandin alone vs combined regimen (all)
Outcome: 01 failure to achieve complete abortion

Study or sub-category	Treatment n/N	Control n/N	RR (fixed) 95% CI	Weight %	RR (fixed) 95% CI	Quality
01 all						
Cheng PGE1&T	36/76	20/75		54.11	1.78 [1.14, 2.77]	A
Creinin M800&MT	16/30	3/31		7.93	5.51 [1.79, 17.00]	A
Jain M800&MI	15/125	5/119		13.77	2.86 [1.07, 7.61]	A
Jain M800&TM	7/75	5/75		13.44	1.40 [0.47, 4.21]	B
Ozeren MP800&MT	15/36	4/36		10.75	3.75 [1.38, 10.21]	A
02 =/< 49 days gestation						
Jain M800&MI	9/80	3/75		100.00	2.81 [0.79, 10.00]	A
03 > 49 days gestation						
Jain M800&MI	6/45	2/44		100.00	2.93 [0.63, 13.76]	A



Methotrexate

- Folic acid antagonist
- Toxic on trophoblast
- Combination with prostaglandin
  - Effectiveness ~ 95 %
- Fetal anomalies

Conclusions - medical methods

- Combined regimes are more effective
- Mifepristone 200 mg seems adequate in the combined regime
- vaginal prostaglandin is more effective compared to oral
- prostaglandin side effects are common

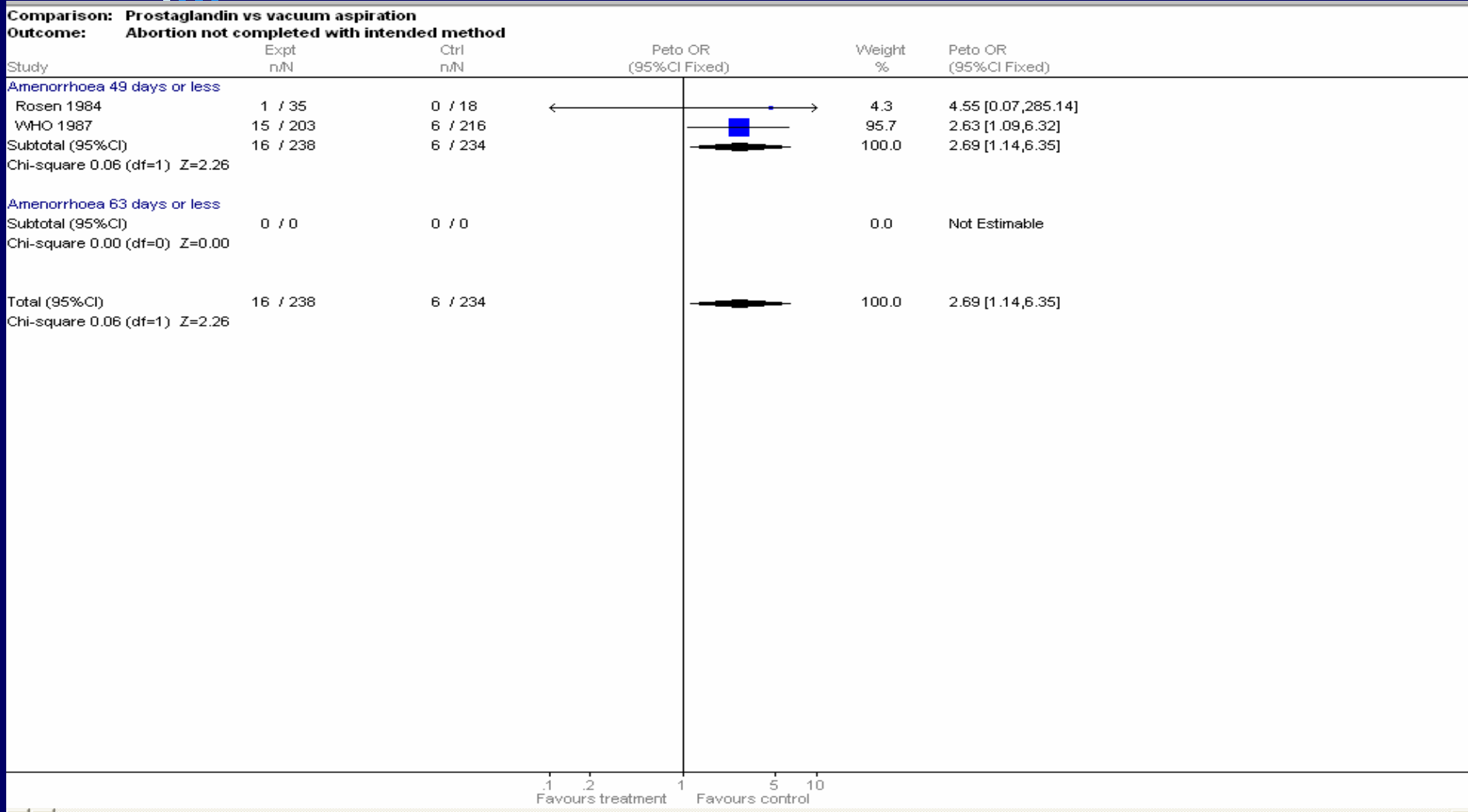
Medical methods - unresolved issues

- No firm conclusion:
  - Effectiveness: dose, type or time of prostaglandin, splitting of dose
  - Acceptability po vs pv
  - Methotrexate: dose, time, route of PG
- Early vs late ?

Medical vs Surgical Say 2002

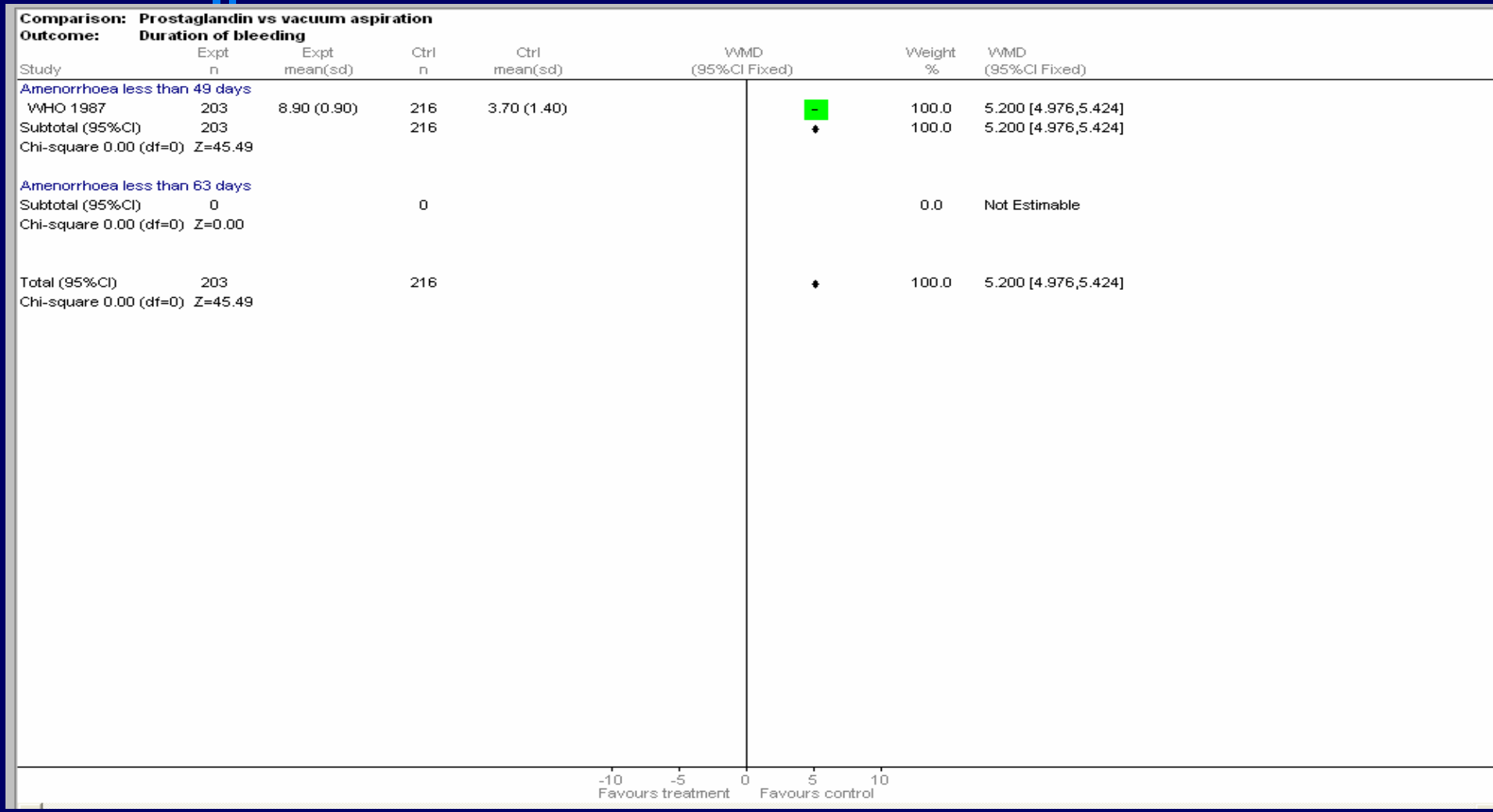
- 5 randomised controlled trials
- 4 comparisons:
  - Prostaglandin vs vacuum aspiration
  - Mifepristone vs vacuum aspiration
  - Mifepristone/prostaglandin vs vacuum aspiration
  - Methotrexate/prostaglandin vs vacuum aspiration

Medical vs surgical Say 2003



Medical vs surgical

Say 2003



Surgical methods

- Vacuum aspiration
- Dilatation/curettage
- Manual vacuum aspiration (MVA)

Surgical methods for first trimester abortion Kulier 2003

- 3 trial included
- 2 comparisons:
  - Vacuum aspiration vs dilatation &curettage
  - Metal vs plastic cannula for vacuum aspiration
- N = 767

Surgical methods for first trimester abortion Kulier 2003

Outcome	No of trials	No of participants	RR (95%CI)
Excessive blood loss	2	257	1.02 (0.21-4.95)
Febrile morbidity	2	467	0.84 (0.26 – 2.71)
Incomplete evacuation	2	467	0.67 (0.11 – 3.95)
Abdominal pain	2	467	2.03 (0.38 – 10.97)

Surgical methods Hemlin 2001

VA vs MVA

- RCT; < 56 days of amenorrhoea
  - MVA n = 91
  - VA n = 88
  - Effectiveness
  - Complications

Surgical methods Hemlin 2001

Outcome	MVA (n=91)	VA (n=88)
Ongoing pregnancy	0	0
Re-curettage	2	2
infection	2	2

Mifepristone

- Second trimester
- Cervical ripening
- Induction of labour
- Postcoital contraception
- Endometriosis/Uterine Leiomyomata
- Hormone dependent tumors
- Antiglucocorticoid action

Medical vs surgical Say 2003

- Small sample sizes
- Medical:
  - Longer duration of bleeding
  - Single regimes less effective than vacuum
- acceptability

Medical vs surgical Henshaw 1994

- n = 363, partially randomised
- < 63 days
- Mifepristone 600 mg/gemeprost 1 mg/ 48 h
- vs
- Vacuum aspiration

Medical vs surgical Henshaw 1994

	Medical n = 172	Vacuum aspiration n = 191	95% CI for difference between proportions
Complete abortion	94.2%	97.9%	-0.003 to 0.078
Minor complications within	11.0%	15.7%	-0.116 to 0.023
Requiring uterine curettage	5.8%	2.1%	

Conclusions

- Safe and effective methods for first trimester abortion are available
- Acceptability data scarce
- Medical methods:
  - Longer duration of bleeding
  - Single regimes less effective
- Serious complications are rare

Collaborators

- Linan Cheng
- Anis Feki
- Metin Gülmezoglu
- Justus Hofmeyr
- Lale Say

International Conference on Population and Development

In circumstances where abortion is not against the law… to ensure that abortion is safe and
accessible."
(Key actions ICPD+5, paragraph 63)

"In all cases,
women should have
access to quality services for the management of complications arising from abortion."
(Key actions ICPD+5, paragraph 63)

•F1. Promote policy dialogue on unsafe abortion, and provide guidance to countries on how to develop, implement and evaluate programmes to prevent and address unsafe abortion.

•F2. Promote the effective management of abortion complications and postabortion care, including its integration within other reproductive health services.

•F3. Develop and promote interventions to improve access to quality care in circumstances where abortion is not against the law, with special emphasis on underserved populations.

UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP)

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